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# THE REACTION OF *B*-ALKYL-9-BORABICYCLO[3.3.1]NONANES WITH ALDEHYDES AND KETONES. A FACILE ELIMINATION OF THE ALKYL GROUP BY ALDEHYDES *

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## Summary

Certain *B*-alkyl-9-borabicyclo[3.3.1]nonanes (9-BBN) reduce benzaldehyde to benzyl alcohol under exceptionally mild conditions. Factors which contribute to a high rate of reaction include: an increase in the degree of substitution at the position $\beta$ to the boron (isobutyl > 1-butyl >> ethyl), the ability of the alkyl group to form a *syn*-planar B—C—C—H conformation (cyclopentyl ≃ norbornyl > sec-butyl >> cyclohexyl), and the presence of an electron-withdrawing *para*-substituent on the benzaldehyde ($p$-Cl > $p$-H > $p$-$CH_3O$). The *B*-alkyl group is transformed into an olefin as the benzaldehyde is reduced. Elimination takes place predominantly if not exclusively towards the more highly substituted $\beta$ hydrogen. The reaction obeys second order kinetics. The observations are consistent with a cyclic mechanism rather than a dehydroboration-reduction pathway.

## Introduction

We have recently reported that certain organoboranes undergo a facile dealkylation when treated with benzaldehyde ***. The reaction can occur rapidly at room temperature. This behavior is highly unusual for alkylboranes which are well noted for their tolerance of functional groups [2].

It has been reported that trialkylboranes will reduce benzaldehyde at elevated temperatures (eq. 1) [3]. The reaction may be performed at lower temperatures (refluxing tetrahydrofuran (THF), 65°C) but requires about 24 h for

$$(C_4H_9)_3B + C_6H_5CHO \xrightarrow[\text{neat}]{100-150^\circ C} (C_4H_9)_2BOCH_2C_6H_5 + CH_2{=}CHC_2H_5 \qquad (1)$$

* We wish to dedicate this paper to Professor H.C. Brown for his pioneering work in the organoborane field.

** A.P. Sloan Foundation Fellow, 1978—1980.

*** A preliminary account of some of this work has appeared [1].

completion. The use of the sterically less hindered *B*-n-butyl-9-BBN is of no advantage. The reaction still requires about 20 h for completion [4]. The reaction should be very favorable due to the transformation of the boron—carbon bond to a boron—oxygen bond. However, the elevated temperatures or prolonged reaction times make this reaction impractical for organic synthesis. Herein we delineate the important factors which contribute to a high rate of dealkylation and address the problem of the mechanism for the reduction.

## Results

*Dealkylation of various B-alkyl-9-BBN compounds with benzaldehyde*

The rate of dealkylation is remarkably dependent upon both the number and nature of β-substituents and the number of α-substituents on the *B*-alkyl group (Table 1). The reaction rate drastically increases with increasing substitution at the position β to the boron. *B*-Ethyl-9-BBN is a very poor reducing agent and requires nearly four days to effect 50% reduction of benzaldehyde. *B*-Alkyl-9-BBN's with a secondary β hydrogen (n-octyl) react much faster, about 50% in 2 h. A β-phenyl substituent has nearly the same effect as a β-alkyl substituent. *B*-Alkyl-9-BBN's containing an alkyl group with a tertiary β hydrogen, such as isobutyl, are very effective reducing agents. Incorporation of one methyl substituent in the α position has a slight positive effect on the rate (compare sec-butyl and 3-methyl-2-butyl to n-octyl and isobutyl). However, incorporation of a second α methyl, as in 2,3-dimethyl-2-butyl-9-BBN, causes a drastic reduction in the rate. In this case the reaction requires nearly 5 days to reach 50% completion.

Cyclopentyl-9-BBN, *exo*-norbornyl-9-BBN, and cyclooctyl-9-BBN react exceptionally fast in comparison to acyclic secondary alkyl 9-BBN's. Cyclohexyl-9-BBN on the other hand is much slower. A tertiary β hydrogen once

TABLE 1

THE DEALKYLATION OF VARIOUS *B*-ALKYL-9-BBN COMPOUNDS BY BENZALDEHYDE

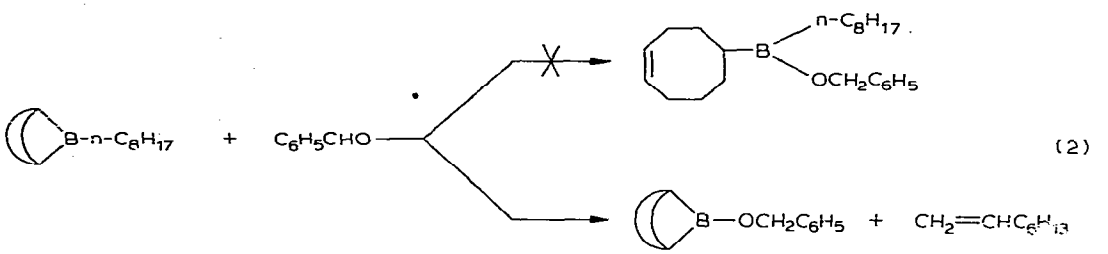
| Alkyl group [a] | $t_{1/2}$ (min) [b] |
|---|---|
| Ethyl | 5500 |
| n-Octyl | 116 |
| 2-Phenylethyl | 98 |
| sec-Butyl | 80 |
| Isobutyl | 21 |
| 3-Methyl-2-butyl | 11 |
| 2,3-Dimethyl-2-butyl | 7000 |
| Cyclopentyl | 15 |
| *exo*-Norbornyl | 20 |
| Cyclohexyl | 420 |
| Cyclooctyl | [c] |
| *trans*-2-Methylcyclopentyl | [c] |
| *trans*-2-Methylcyclohexyl | 67 |
| 4-Isocaranyl | [c] |
| 1,2-Dimethylcyclopentyl | 1000 |

[a] 0.5 *M* *B*-Alkyl-9-BBN in THF at 65°C. [b] Time for 50% completion of the reaction. [c] The reaction was too fast to measure accurately.

again increases the rate. In the case of *trans*-2-methylcyclopentyl-9-BBN or 4-isocaranyl-9-BBN the reaction is so fast that it cannot be followed by VPC. It is over within a few minutes in refluxing THF. *trans*-2-Methylcyclohexyl-9-BBN has a rate comparable to that of acyclic secondary boranes. An $\alpha$ methyl on the ring (1,2-dimethylcyclopentyl-9-BBN) dramatically decreases the rate but not as much as was noted for 2,3-dimethyl-2-butyl-9-BBN.

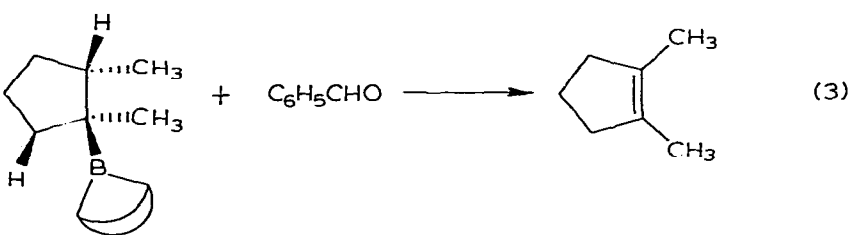
*Selectivity of the olefin displacement*

*B*-n-Octyl-9-BBN could in principle react with benzaldehyde by displacement of the cyclooctyl ring to give a cyclooctenyl derivative or by displacement of the octyl group to give 1-octene (eq. 2). In practice, for each mol of benzaldehyde consumed, 1 mol of 1-octene is produced. We have seen no participation by the cyclooctyl ring.



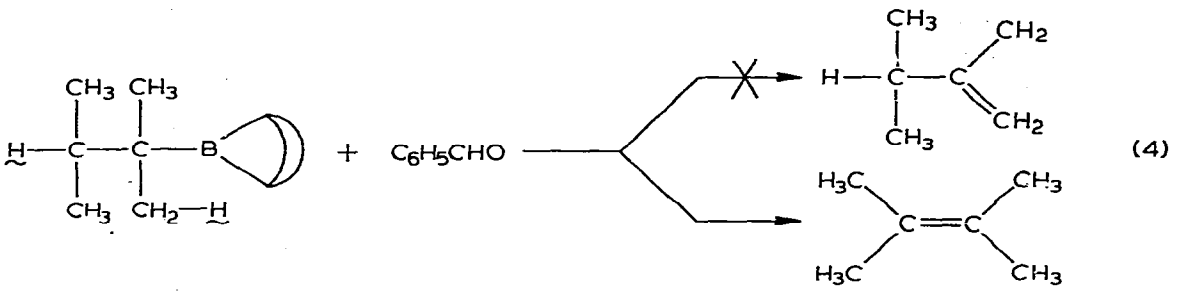
(2)

As mentioned, alkyl groups containing a tertiary $\beta$ hydrogen generally reduce benzaldehyde much faster than do alkyl groups containing a primary or secondary $\beta$ hydrogens. The greater reactivity of the tertiary hydrogen also manifests itself in the regiochemistry of the olefin which is eliminated. The elimination invariably occurs towards the more highly substituted hydrogen. Thus 2-butyl-9-BBN gives exclusively 2-butene (a 65/35, *trans/cis* ratio) and 3-methyl-2-butyl-9-BBN gives 2-methyl-2-butene. Even in the case of *trans*-2-methylcyclopentyl-9-BBN and 1,2-dimethylcyclopentyl-9-BBN where a tertiary and a secondary $\beta$ hydrogen compete for elimination, only 1-methylcyclopentene and 1,2-dimethylcyclopentene are formed (eq. 3). Finally in the case of 2,3-dimethyl-2-butyl-9-BBN elimination could occur toward the tertiary hydrogen



(3)

or towards the primary hydrogen (eq. 4). One would expect a 6/1 statistical ratio in favour of the latter based on the number of $\beta$ hydrogens. However, only 2,3-dimethyl-2-butene is detected. In each of these cases the original olefin which was hydroborated is regenerated during the reduction and the original hydride on the 9-BBN is transferred to the benzaldehyde.




(4)

*Kinetics and isotope effect*

Benzaldehyde was reduced by an equal molar amount of *B*-n-octyl-9-BBN and the reaction progress was followed by the appearance of 1-octene. A plot of the data indicated that the reaction followed second order kinetics with a rate constant of $4.1 \times 10^{-5}$ l $m^{-1}$ $s^{-1}$ at 25°C.

1-Octene was deuteroborated with 9-BBN-9-*d*. The resulting *B*-n-octyl-9-BBN was then treated with benzaldehyde. Analysis of the benzyl alcohol for deuterium indicated a kinetic isotope effect of 2.57.

*Effect of the aldehyde or ketone*

The rate of reduction is affected by *para*-substituents on the benzaldehyde (Table 2). In general, electron-donating groups slow the reaction while electron-withdrawing groups speed the reaction. In competition experiments we have found the following order of reactivity: *p*-$NO_2$ > *p*-Cl > *p*-H > *p*-$OCH_3$ > *p*-N-$(CH_3)_2$. All aldehydes investigated, except those with strongly electron-donating groups, are reduced with ease by *B*-3-methyl-2-butyl-9-BBN.

TABLE 2

THE DEALKYLATION OF *B*-n-OCTYL-9-BBN WITH SUBSTITUTED BENZALDEHYDES

| Substituent [a] | $t_{1/2}$ (min) [b] |
|---|---|
| *p*-Chloro | 90 |
| *p*-Hydrogen | 180 |
| *p*-Methoxy | 720 |

[a] 0.35 *M* *B*-n-Octyl-9-BBN in THF at 65°C. [b] Time for 50% completion of the reaction.

TABLE 3

THE REACTION OF KETONES WITH *B*-ALKYL-9-BBN

| Alkyl-9-BBN [a] | Ketone [a] | $t_{1/2}$ (min) [b] |
|---|---|---|
| 3-Methyl-2-butyl | Cyclohexanone | 1800 |
| 3-Methyl-2-butyl | Cyclopentanone | 1200 |
| 3-Methyl-2-butyl | Acetophenone | 1275 |
| Isobutyl | Acetophenone | 4000 |
| *trans*-2-Methylcyclopentyl | Acetophenone | 4180 |
| Cyclopentyl | Acetophenone | [c] |
| n-Butyl | Acetophenone | [c] |

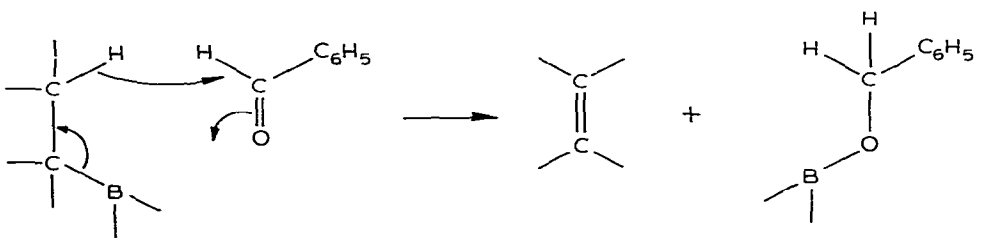
[a] 0.5 *M* in THF at 65°C. [b] Time for 50% completion of the reaction. [c] The reaction was very slow.

Although aldehydes are reduced rapidly, ketones are reduced only very sluggishly (Table 3). For example, 3-methyl-2-butyl-9-BBN reduces benzaldehyde by 50% in 11 minutes but requires nearly 22 h to reduce acetophenone by 50%. The reduction rate of ketones may be increased by increasing the *B*-alkyl-9-BBN concentration.

## Discussion

We have found that the use of *B*-alkyl-9-BBN compounds containing a tertiary $\beta$ hydrogen dramatically increases the rate of reduction of benzaldehyde. With conventional trialkylboranes this is a rather slow process which requires elevated temperatures or prolonged reaction times. Such a dramatic increase in reaction rate is not observed for the trialkylboranes. Mikhailov reported [3] that triisobutylborane requires slightly lower temperatures than tri-n-butylborane and in a competition experiment with tri-n-propylborane gives 62% isobutylene and 38% propene. He also found that tri-sec-butylborane is slower than tri-n-butylborane. The dramatic increase in rate for the *B*-alkyl-9-BBN compounds may be attributed to a decrease in the steric hindrance around boron in these compounds [5]. Thus the substituents on the alkyl group can have a greater effect on the rate.

Mikhailov has proposed a cyclic mechanism for the reduction of benzaldehyde by trialkylboranes (eq. 5) [3]. Such a cyclic process has also been proposed for




(5)

the reaction of trialkylboranes with *cis*-azobenzene [6], 2-methyl-2-nitrosopropane [7], and formaldehyde [8]. However, cyclooctyl—boron bonds are exceptionally prone to undergo boron migration, presumably by a dehydroboration—hydroboration process [9]. Indeed, cyclooctyl-9-BBN is dealkylated with exceptional ease. Thus the *B*-alkyl-9-BBN reductions could occur by either eq. 5 or 6. The facts are consistent only with the cyclic process. The reaction occurs under

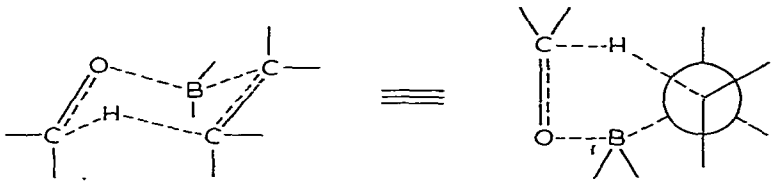
$$R_3B \xrightarrow[\text{slow}]{\Delta} R_2BH + \text{olefin} \xrightarrow[\text{fast}]{C_6H_5CHO} R_2BOCH_2C_6H_5 \qquad (6)$$

much milder conditions than are normally required for dehydroboration. We have found that the reaction can occur rapidly at room temperature. The reaction obeys second-order kinetics as required for the bimolecular cyclic mechanism and the rate is affected by the structure of the ketone or aldehyde. These results are in accord with a hydride transfer to the carbonyl in the transition state. Only the *B*-alkyl group is eliminated even though cyclooctyl elimination is extremely favorable. Finally, the high enantioselectivity observed for these reductions using *B*-pinanyl-9-BBN [10] suggests that a B—H compound is not the

reducing agent but that the pinanyl group is playing an important role in the reduction.

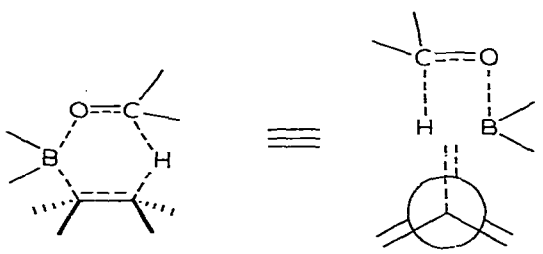
One may envision two extremes for the transition state of the reduction. The first (Scheme 1) invokes a chair-like transition state. Such a transition state has

SCHEME 1



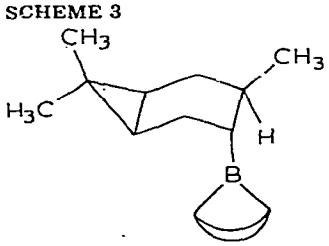
been proposed to account for certain stereoselectivities in the reduction of alkyl phenyl ketones by Grignard and other reagents [11]. The other transition state extreme would be a planar arrangement as indicated in Scheme 2.

SCHEME 2



Models indicate that for the rigid bicyclo[3.3.1]nonane ring to react, only the chair-like transition state is possible. The *B*-alkyl group, on the other hand, is free to rotate and assume the planar structure. Such a situation would allow maximum overlap of orbitals in the developing $\pi$ system of the displaced olefin. The ability to form a planar arrangement of the B—C—C—H bonds plays an important role in determining the rate of reduction. Thus cyclopentyl-9-BBN and *trans*-2-methylcyclopentyl-9-BBN are exceptionally fast. Cyclohexyl-9-BBN and *trans*-2-methylcyclohexyl-9-BBN on the other hand are unusually slow. To form a planar arrangement these compounds must be in a boat conformation. However, the reaction is much faster with 4-isocaranyl-9-BBN which also contains the *trans*-2-methylcyclohexyl ring system (Scheme 3). In this case the rigid cyclopropane ring makes the boat form more favorable.

SCHEME 3



Norbornene (as well as ethylene) has been shown to be dehydroborated from organoboranes rather slowly [12]. This slowness has been attributed to the high energy (as measured by heats of hydrogenation) of these olefins. However, we have found that norbornene is displaced rapidly by benzaldehyde. Once again the planar B—C—C—H arrangement in *B-exo*-norbornyl-9-BBN is important.

2,3-Dimethyl-2-butyl-9-BBN, although containing a tertiary $\beta$ hydrogen reacts exceptionally slowly with benzaldehyde. This is rather surprising in view of the ease of displacement of 2,3-dimethyl-2-butene from boron in a number of cases [13]. However, in these cases the displacement occurs in the presence of boron—hydride species which may catalyze the reaction. In the present case the slowness of the reaction may be attributed to either the steric blocking of boron by the large alkyl group or the inability of the alkyl group to assume the planar arrangement due to the eclipsing of the four methyl groups. Both of these factors seem to be important. 1,2-Dimethylcyclopentyl-9-BBN in which the B—C—C—H bond is held more or less planar is faster than 2,3-dimethyl-2-butyl-9-BBN. However the rate is much slower than the less crowded cyclopentyl-9-BBN.

We have noted that elimination occurs predominantly towards the more highly substituted hydrogen. The greater reactivity of the tertiary hydrogen is in agreement with the transfer of a hydride to the carbonyl. However, the extremely high regioselectivity of the reaction is rather surprising. Perhaps the biggest surprise is the regioselectivity displayed by 1,2-dimethylcyclopentyl-9-BBN. In this case the relatively hindered tertiary hydride must compete for a secondary cyclopentyl hydride which has been shown to undergo a very facile elimination. This high degree of selectivity has not been observed in other dealkylations. Mikhailov [3] reported that tri-sec-butylborane gives a 93/7 mixture of 2-butene and 1-butene. Davies has reported that the organoborane from *cis*-3-methyl-2-pentene gives an approximately 70/30 mixture of 3-methyl-2-pentene and 3-methyl-1-pentene with azobenzene [6] and Roberts a 33/67 mixture of these olefins with 2-methyl-2-nitrosopropane [7]. The electronic and steric factors controlling the direction of olefin formation remain to be explored. However, the high regioselectivity of the dealkylation combined with the selectivity of the hydroboration reaction suggests that this may be a good method for protecting olefins.

## Experimental

*General comments*

All operations were performed under a dry nitrogen atmosphere using the techniques described in Chapter 9 of ref. 2c. All glassware was dried at 135°C for at least 4 h, assembled hot and cooled while being purged with nitrogen. Reaction flasks were fitted with rubber septa for the introduction of reagents using syringe or double-ended needle techniques. Gases were delivered using a gas-tight syringe [14]. All reactions were stirred under a static nitrogen atmosphere using Teflon-coated magnetic stirring bars.

THF was distilled under nitrogen from benzophenone ketyl and stored under a positive nitrogen pressure. Olefins were obtained commercially and were distilled from a small quantity of lithium aluminium hydride under nitrogen. Liquid aldehydes were distilled before use. Solid aldehydes were dissolved in a small

quantity of THF and added by syringe. Solid 9-BBN was prepared by the method of Brown [15] and was dissolved in THF to make a 0.5 *M* solution.

VPC analyses were carried out on a Hewlett—Packard 5732 thermal conductivity gas chromatograph using normal hydrocarbons as internal standards. Peak integrations were obtained using a Linear Instruments model 252 integrating recorder. Routine analyses were performed on a 6 foot × 1/8 inch stainless steel column filled with 10% DC710 on AW DMCS 100/120 Chromosorb W. Butenes were analyzed on a 6 foot × 1/8 inch 10% $AgNO_3$/benzyl cyanide column on Chromosorb P. The methylcyclopentene isomers were analyzed on a 6 foot × 1/8 inch 10% oxydipropionitrile column. NMR spectra were recorded on a Varian EM390 (90 MHz) spectrometer.

*General procedure*

A 50 ml flask equipped with a reflux condenser and connected to a mercury bubbler was flushed with nitrogen and charged with 5 mmol of 9-BBN in THF. The olefin was added and the solution stirred at room temperature or reflux for the appropriate time [15]. A hydrocarbon internal standard was added, and the solution analyzed for remaining olefin. The solution was then refluxed and 5 mmol of the aldehyde added. The progress of the reaction was followed by VPC. The time to reach 50% completion for various alkyl groups is reported in Table 1.

*Olefin analysis*

The reaction was run as above. After hydroboration a vacuum was pulled on the flask to remove excess starting olefin, the THF replaced and the reaction continued. After completion of the reaction the solution was cooled to room temperature and oxidized by the addition of 1.7 ml of 3 *N* sodium hydroxide followed by 1.7 ml of 30% hydrogen peroxide. The solution was stirred at 50°C for 15 min, cooled and saturated with $K_2CO_3$. The THF layer was then analyzed by VPC for the olefin. In the case of sec-butyl-9-BBN the butenes were collected in a trap containing THF maintained at —78°C which was placed between the reflux condenser and the mercury bubbler. The butenes were swept from the reaction flask by a slow stream of nitrogen.

*Kinetics*

*B*-n-Octyl-9-BBN, 5.00 mmol, was prepared as usual. The solvent and excess 1-octene were removed under vacuum. The borane was transferred in THF to a 10 ml volumetric, dodecane was added as an internal standard and the flask equilibrated in a constant temperature bath. Freshly distilled benzaldehyde, 5.00 mmol, was added to the flask and the solution diluted to 10.0 ml. The solution was analyzed by VPC for 1-octene formation. A plot of $1/([\text{octene}]_\infty - [\text{octene}])$ versus time gave a straight line ($\beta$ of 0.995) with a slope of $4.10 \pm 0.20 \times 10^{-5}$ l $m^{-1}$ $s^{-1}$ for two runs at 25°C.

*Isotope effect*

1-Octene, 0.31 ml, was deuteroborated with 4.00 ml of a 0.5 *M* solution of 9-BBN-9-*d* [16] in THF (2 h at reflux). The 9-BBN-9-*d* contained 85.8% deuterium as analyzed by benzaldehyde reduction. Freshly distilled benzaldehyde, 0.24 ml, was added and the solution stirred until no more 1-octene appeared. The

THF was removed with a water aspirator and the excess benzaldehyde removed with a vacuum pump. Ethyl ether, 3.5 ml, was added followed by 0.14 ml of ethanolamine. The solution was cooled to 0°C and the white precipitate removed by filtration. The ether was concentrated and the residue distilled by Kugelrohr (25 mmHg, 100°C pot). Analyses by NMR of the benzyl alcohol indicated a deuterium content of 24% (28% corrected for deuterium content of the 9-BBN-9-*d*). This value gives a $K_H/K_D$ of 2.57.

*Competition experiments*

*B*-n-Octyl-9-BBN, 5 mmol, was prepared in THF. A mixture of benzaldehyde, 5 mmol, and a second aldehyde, 5 mmol, in THF was added to the 9-BBN. An aliquot was removed and added to a nitrogen-flushed NMR tube. The sample was then analyzed by integrating the aromatic and aldehydic protons to obtain the ratio of remaining aldehyde. The general order of reactivity was found to be: $p\text{-}NO_2 > p\text{-}Cl > p\text{-}H > p\text{-}OCH_3 > p\text{-}N(CH_3)_2$.

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